(2)

AD-A224 406

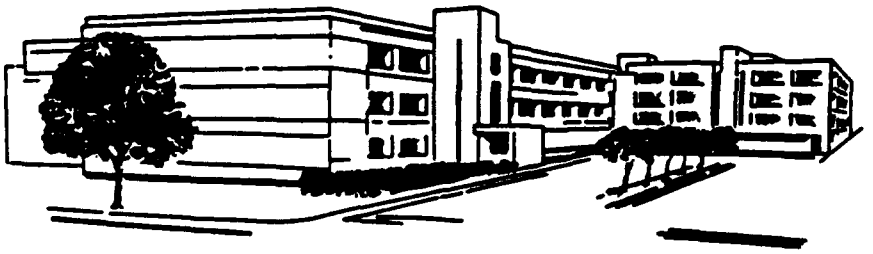
INSTITUTE REPORT NO. 450

The Centriole in Photoreception

E. Manougian, H. Zwick and S. Schuschereba

Division of Ocular Hazards Research

April 1990



LETTERMAN ARMY INSTITUTE OF RESEARCH PRESIDIO OF SAN FRANCISCO CALIFORNIA 94129

This material has been reviewed by Letterman Army Institute of Research and there is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. *(AR 360-5)*

Donald G Corby 20 April 90

DONALD G. CORBY (date)
COL, MC
Commanding

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION: UNCLASSIFIED	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT: UNLIMITIED DISTRIBUTION
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S): Institute Report No. 450	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION: Letterman Army Institute of Research; 6b. OFFICE SYMBOL (If applicable): SGRD-ULY-OH	7a. NAME OF MONITORING ORGANIZATION: US Army Medical Research and Development Command
6c. ADDRESS (City, State, and ZIP Code): Letterman Army Institute of Research, Division of Ocular Hazards, Presidio of San Francisco, CA 94129-6800	7b. ADDRESS (City, State, and ZIP Code): Fort Detrick, Frederick, MD 21701-5012
8a. NAME OF FUNDING/SPONSORING ORGANIZATION; 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c. ADDRESS (City, State, and ZIP Code)	10. SOURCE OF FUNDING NUMBERS: PROGRAM ELEMENT NO. 61102A; PROJECT NO. 3M61102 BS15; TASK NO. CF; WORK UNIT ACCESSION NO. DA0E6078

11. TITLE (Include Security Classification)

(U) The Centriole in Photoreception

12. PERSONAL AUTHOR(S)

Edward Manougian, MD; Harry Zwick, PhD; Steve Schuschereba, MA.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Laboratory	FROM Feb 87 TO May 89	1989, May	20

16. SUPPLEMENTARY NOTATION

17. COSATI CODES		
FIELD	GROUP	SUB-GROUP

18. SUBJECT TERMS (~~Continue on reverse if necessary and identify by block number~~)

Basal bodies, retinal pigment epithelium, ~~low level~~ LASERS, laser exposure, photoreceptors, EYES

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

We recently reported an increase in the number of basal bodies and their associated striated rootlets in the retinal pigment epithelium (RPE) of mammalian eyes exposed to low level chronic laser radiation (1). The significance of this increase in basal body number is unknown. A more conspicuous location of basal bodies is in the rods and cones of the retina where they provide the vital link between the inner segment and outer segment. Furthermore, there is a resemblance between the RPE basal bodies and the photoreceptor basal bodies in that they form part of a primary cilium (2). Since photoreceptors are more readily approached experimentally, a study of the role of the basal body in these cells was initiated.

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT: ☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS	21. ABSTRACT SECURITY CLASSIFICATION: UNCLASSIFIED
22a. NAME OF RESPONSIBLE INDIVIDUAL: DONALD G. CORBY, COL, MC	22b. TELEPHONE (Include Area Code): (415) 561-6300; 22c. OFFICE SYMBOL: SGRD-ULE-Z

DD Form 1473, JUN 86 *Previous editions are obsolete.*

SECURITY CLASSIFICATION OF THIS PAGE

UNCLASSIFIED

ABSTRACT

This paper presents a novel concept using the analogy of the physical structure of the magnetron contrasted with the centriole. A sodium current drives the centriole in a manner similar to the electron current in the magnetron. Electromagnetic phenomenon arising from centriole activity in the connecting cilium of the photoreceptor acts as a filter to reduce noise effects in photoreception. Similar electromagnetic phenomena are proposed for centrioles in other cells.

THE CENTRIOLE IN PHOTORECEPTION, I

INTRODUCTION

We recently reported an increase in the number of basal bodies and their associated striated rootlets in the retinal pigment epithelium (RPE) of mammalian eyes which had been exposed to low level chronic laser radiation (1). The significance of this increase in basal body number is unknown. A more conspicuous location of basal bodies is in the rods and cones of the retina where they provide the vital link between the inner segment and outer segment. Furthermore, there is a resemblance between the RPE basal bodies and the photoreceptor basal bodies as they form part of a primary cilium (2). Since photoreceptors are more readily approached experimentally, we chose to study the role of the basal body in these cells. To establish the terminology, a basal body is a centriole located at the base of a cilium with another centriole associated with it. This complex of centriole, basal body, and cilium will be called a centriole-basal body-cilium complex (CBBC).

This note proposes a hypothesis regarding the role of the centriole-basal body-cilium complex in mammalian photoreceptors and RPE, suggesting that cells with centrioles sustain electronic and electromagnetic oscillatory phenomena, similar to processes seen in microwave-producing electronic devices, i.e., magnetrons. We propose oscillatory phenomena of this nature play a role in the operation of the centriole-basal body-cilium complex. After briefly discussing the essential features of magnetrons, we review centriole structure and photoreceptors, then offer a proposal regarding the function of the CBBC complex in photoreception.

MAGNETRONS

Structural Similarities between Magnetrons and Centrioles

Centrioles are found in all animal cells and some lower plant eukaryotic cells (3). The general uniformity in structure of the centriole in this great variety of cells is quite striking. Basically, this structure consists of nine sets of three tubules arranged in a CYLINDRICAL fashion. When viewed in cross section, one end of the cylinder may have a CARTWHEEL arrangement of electron dense material (3).

This same cylindrical pattern is seen in one form of the magnetron which consists of two concentric CYLINDERS. When such a magnetron is in a certain mode of oscillation, a CARTWHEEL arrangement of electrons appears in the space between the cylinders (4). While centriole function and modus operandi remain unknown, magnetron function and modus operandi are fairly well understood. We propose that understanding one will lead to an understanding of the other.

Magnetron Structure

Interestingly, magnetrons vary a great deal in structure. The two basic types of magnetrons are the M-type and the O-type (5). The M-type of magnetron (M-magnetron) utilizes both an electric and a magnetic field to produce oscillations whereas the O-type magnetron (O-magnetron) utilizes a slow wave structure (which may be a helix) and a flow of electrons. In either type, M-magnetrons or O-magnetrons, energy in the form of electromagnetic waves is emitted perpendicular to the cylinder axis. Interestingly, new centrioles form perpendicular to the parent centriole from materials not originating with the parent centriole. Electromagnetic energy may guide this process, and the wavelength of this radiation may determine the length of the new centriole.

M-magnetrons

The essential components of an M-magnetron are two parallel conductors. A constant electric field is applied to the parallel conductors; a constant magnetic field is applied orthogonal to the electric field and parallel to the surface of the conductors (Figure 1).

Most M-magnetrons are cylindrical. However, biologically, all forms of M-magnetron behavior may be operational; viz., membranes could conceivably operate in the planar fashion and neuronal conduction in the coaxial fashion. Centriole operation of the M-type would be either by the cylindrical method or the coaxial method since its general shape is cylindrical. Since the electric and magnetic fields are orthogonal, these tubes are called crossed-field devices.

The gap between the two conductors is the interaction space where electrons emitted from the cathode interact with the constant electric and magnetic fields to produce an electromagnetic field. This electromagnetic field is si-

phoned off perpendicular to the cylinder axis and has a frequency commensurate with the physical dimensions of the magnetron. During interaction of the electrons with the electric and magnetic fields, various groupings of the electrons occur depending upon the magnetron's mode of oscillation. In some modes electrons form a cartwheel arrangement.

O-Magnetrons

The O-magnetron is a linear traveling wave tube (TWT) in contrast to the cylindrical M-magnetron where the wave is generally circular, i.e., rotating inside the external cylinder (usually the anode). A common arrangement in the TWT is a linear flow of electrons interacting with a wave traveling in a cylindrical structure often with a helix as the source of the wave (6, 7). Electrons traveling in the direction of the wave but with a velocity slightly greater than that of the wave will "collide" with the wave, thereby increasing the wave momentum and thus its energy, consequently amplifying it. The electrons that collide slow down and, if slowed enough, will be struck by a wave, ultimately becoming bunched. Backward traveling waves may develop from this interaction.

These backward traveling waves carry energy back to the input thereby providing a feedback system; oscillations (standing waves) result. Reflections due to impedance mismatch can also cause backward traveling waves and result in self-induced oscillations. Backward traveling wave oscillators (BWO) using this phenomenon have been constructed (8).

O-magnetrons often have a focusing magnetic or a focusing electrostatic field to maintain the electron flow along the cylinder's axis (7). Space charge effects, essentially mutual repulsion of like negative charges, would necessitate such focusing fields, especially in long tubes. However, in the retinal photoreceptors, the flow is of hydrated sodium ions rather than electrons. Hydration of the positive sodium ions reduces the charge density of the sodium ion flow resulting in less space charge effect (repulsion) thereby reducing the need for focusing.

In the final section of this paper we propose that O-magnetron or BWO type oscillations occur in the basal body of the cilium of retinal photoreceptors.

Uses of Magnetrons

The versatility of magnetrons can be gleaned from their use:

(1) To measure e/M, i.e., the ratio of charge to mass of electrons (8)

(2) To measure magnetic field strength (8)

(3) To cut off electric current (8)

(4) To measure electronic conductance (9)

(5) To measure phase coherence (9)

(6) As an amplifier (10)

(7) As an oscillator for the production of microwaves (10)

(8) To measure electron affinities, electron transfer, electronegativity, stability of negative ions, and surface catalytic rearrangements of hydrocarbons (11)

CENTRIOLES

Centriole Location

Centrioles are minute cytoplasmic organelles barely visible by light microscopy (2). If located at the base of a cilium, the centriole is called a basal body. Centrioles generally occur in pairs, even when one is serving as a basal body, and generally one is perpendicular to the other. When located in the periphery of the cytoplasm near the cell membrane, one centriole usually becomes a basal body and a cilium develops from it (called a secondary cilium); the other centriole remains perpendicular to the basal body. We call this organization of organelles a centriole-basal body-cilium complex (CBBC). In the rods and cones of the mammalian retina there is a single such complex; the cilium is the outer segment of the photoreceptor. Although the conventional role of peripherally located cilia is motion, viz., movement of mucus in the trachea, in the rods and cones the role of CBBC seems to be sensory. Interestingly, cilia can develop entirely within the cytoplasm, their

surrounding membrane coming from vesicles produced by the Golgi apparatus (2). Here the centriole-basal body-cilium complex, called a "primary cilium", is engulfed in the cytoplasm and is thought by some investigators to have a sensory function. The CBBC of photoreceptors possess characteristics of both primary and secondary cilia; although the cilium is at the cell surface as in a secondary cilium, the central pair of tubules which are characteristic of secondary cilia, are absent as in a primary cilium. The effect of chronic low level laser radiation on the RPE noted earlier was the production of an increase in number of primary cilia (1).

Centrally located centrioles need not form cilia. Although centrioles become positioned in the aster bodies of the mitotic spindle, their role in cell division remains unclear. Indeed, in general, centriole function and mode of operation are unknown.

Centriole Structure

The general shape of the centriole is cylindrical. In most cells mature centrioles measure 200 - 250 nm in diameter and 175 - 700 nm in length. From animal to animal, tissue to tissue, diameters tend to be fairly consistent, although lengths can vary from 150 nm (fungal centrioles) to 8000 nm (neuropteran centrioles) (2).

The walls of the cylinder have nine sets of triplet tubules (see Figure 2). Each member of the triplet is a tubule made of molecules of a globular protein arranged in a spiral. The tubule itself is hollow with an inner diameter of 12 - 14 nm and an outer diameter of 20 - 25 nm. The proximal portion of a centriole as frequently seen in cross section is depicted in Figure 2. The distal portion is similar to the proximal portion, but usually lacks the cartwheel appearance within it and the pitch of the triplets is greater, in the vicinity of 60^{o}. Sometimes a vacuole is seen in the center of the distal portion of the centriole.

Although there is some controversy surrounding this concept, the core of the centriole is thought to contain a helical structure having 8 to 10 twists in the total length of the centriole (2). Indeed Stubblefield and Brinkley characterized this internal helix as extending the full length of the centriole. This internal helix has a diameter of 130 nm, spacing of 75 nm/turn and thickness of 5 - 7.5 nm (12). The total stretched length of the helix is 4 - 5

microns (12) and evidence indicates that this helix is RNA or ribonucleoprotein (2).

Centriole Development

Eventually, near one end of the centriole, a second "daughter" centriole develops perpendicular to the axis of the original ("parent") centriole, usually at a distance of 90 - 110 nm from it, but this distance may vary from 25 to 150 nm (2, 13). This daughter centriole may not reach full length until later in the cell's history. In this primordial form it is called a procentriole. Nonetheless, it remains perpendicular to the parent centriole held by an unknown force until ready to serve as a parent by reaching full size and positioning parallel to its parent. When cells are forming a ciliated border, more than one centriole may form from the parent centriole at any one time; each new centriole will be perpendicular to the parent.

RNA is involved in the development of new centrioles (14, 15). Since RNA has been noted in the core of the centriole, it appears that the RNA involved in the development of the centriole remains as part of the centriole, probably comprising the helix inside the core as noted earlier. This renders the centriole structurally similar to an O-magnetron of the backward wave type. Centrioles serving as basal bodies may also arise de novo from dense material similar in appearance to the material of the immature procentriole (2). De novo synthesis of this sort is most apt to occur when there is an immediate need for many basal bodies in the formation of cilia. Their development occurs synchronously. Other stimuli for the formation of increased numbers of centrioles are (1) electric current (16), (2) pargyline (17), (3) furosemide in combination with colchicine (posterior lobe of rat pituitary) (18), and (4) laser light (1) (in the retinal pigment epithelium).

Chemical Composition of Centrioles (2)

The chemical composition of centrioles is not fully known. Evidence suggests that they contain no DNA. As noted earlier, moderate amounts of RNA have been found in this organelle (2, 16). A considerable amount of protein and the elements S, Cl, and K are present. Surprisingly, Si has been noted in the centriole. Furthermore, steroids have been implicated in centriole structure (19).

Centriole Associated Structures (2)

The homogeneous region surrounding nonciliated centrally located centrioles consists of microfilaments and fibers lightly bound to one another to form a stable and rather incompressible spherical body. Usually this pericentriolar matrix extends to a radius of 200 - 1000 nm around the pair of centrioles. Primary and secondary cilia are not embedded in such a matrix, but do have filamentous and microtubular structures associated with them and, in the case of secondary cilia, with the cell membrane as well.

There are various centriole-associated structures having a periodic appearance. These include the so-called "rootlets" or "striated feet" with a periodic banding pattern of dense bands alternating with light bands (on electron microscopy) in intervals of 45 - 75 nm. In the rods and cones, rootlets can extend from the basal body of the connecting cilium to the nucleus and beyond (20-22). The main protein of the rootlets is ankryrin with electrophoretic peaks at 230,000 Daltons and 250,000 Daltons. The striations suggest a muscular action or represent waves in the protein. At times the two centrioles are linked to one another, still at right angles to each other, by such striated feet although the orthogonal orientation is not due to the striated feet. Such linking seems to occur only in instances when one of the centrioles in the pair forms a primary cilium.

In addition, the Golgi apparatus which has the physical appearance of condenser plates, sometimes comes to within 20 - 30 nm of the centriole. In the formation of primary cilia the Golgi apparatus creates vacuoles which engulf the cilium forming a sheath around it and giving the cilium a general appearance similar to the outer segment of the rods and cones of the retina.

Centriole-Basal Body-Cilium of Photoreceptors

In mammalian photoreceptors, the pair of centrioles occupy a crucial position. One centriole serves as the basal body for the connecting cilium, which appears to be the major link between the outer segment (OS) and the inner segment (IS), while the other centriole sits perpendicular to this basal body. Typical of primary cilia but in contrast to secondary or motile cilia, the central pair of tubules present in motile cilia are lacking in the connecting cilium (2, 23).

What passes through the center of the connecting cilium is yet unclear. For instance, although opsin, the protein of rhodopsin, is produced in the myoid of the IS, it does not pass through the cytoplasm of the connecting cilium to reach the OS. It appears that some, if not all of the opsin, passes by way of the plasma membrane of the cilium (23).

Since the connecting cilium and its associated basal body and centriole are in a critical position in these mammalian photoreceptors, a proposal regarding their possible role in the process of photoreception will be made at the conclusion of this paper. First, the cell biology of these photoreceptors will be reviewed.

MAMMALIAN PHOTORECEPTION

Since retinal rods have been studied more extensively than retinal cones, this presentation applies specifically to rods unless otherwise stated.

Anatomy of Rods and Their Environment

The retinal rod consists basically of seven regions. Proceeding from the synaptic terminal, which is in contact with bipolar and horizontal cells, are the fiber, the nucleus, the myoid, the ellipsoid (rich in mitochondria), the connecting cilium, and the disk laden outer segment (ROS), which is in contact with the retinal pigment epithelium (RPE) (20). The portion of the rod which extends from the synaptic terminal to the connecting cilium is called the rod inner segment (RIS). In the ROS, the disks are separate from the cell's plasma membrane (except for a few new ones near the cilium), but in the cone's outer segment, the disks are evaginations of the plasma membrane (23). The basal body of the cilium is accompanied by a centriole generally perpendicular to it. The mitochondria of the ellipsoid are dispersed radially from the centriole. The rootlets from the basal body may extend as far as the nucleus. Indeed, Spira et al (22) have seen cross-striated fibrils extending from the rootlets to the synaptic terminal. They present histochemical evidence that these fibrils have an energy-utilizing contractile function. Others have shown that rootlets exhibit a calcium induced contraction and contain a spasmin-like protein (24). In addition to these cross-striated fibrils, there are actin filaments extending from the cytoplasmic collars to the synaptic region and appear to

be involved in rod elongation and contraction in some animals (24).

There are no inhibitory connections (synapses) in photoreceptors. They, therefore, must provide their own inhibitory mechanism. The centriole-basal body-cilium complex may play a role in this control.

Biochemistry and Physiology of Photoreception

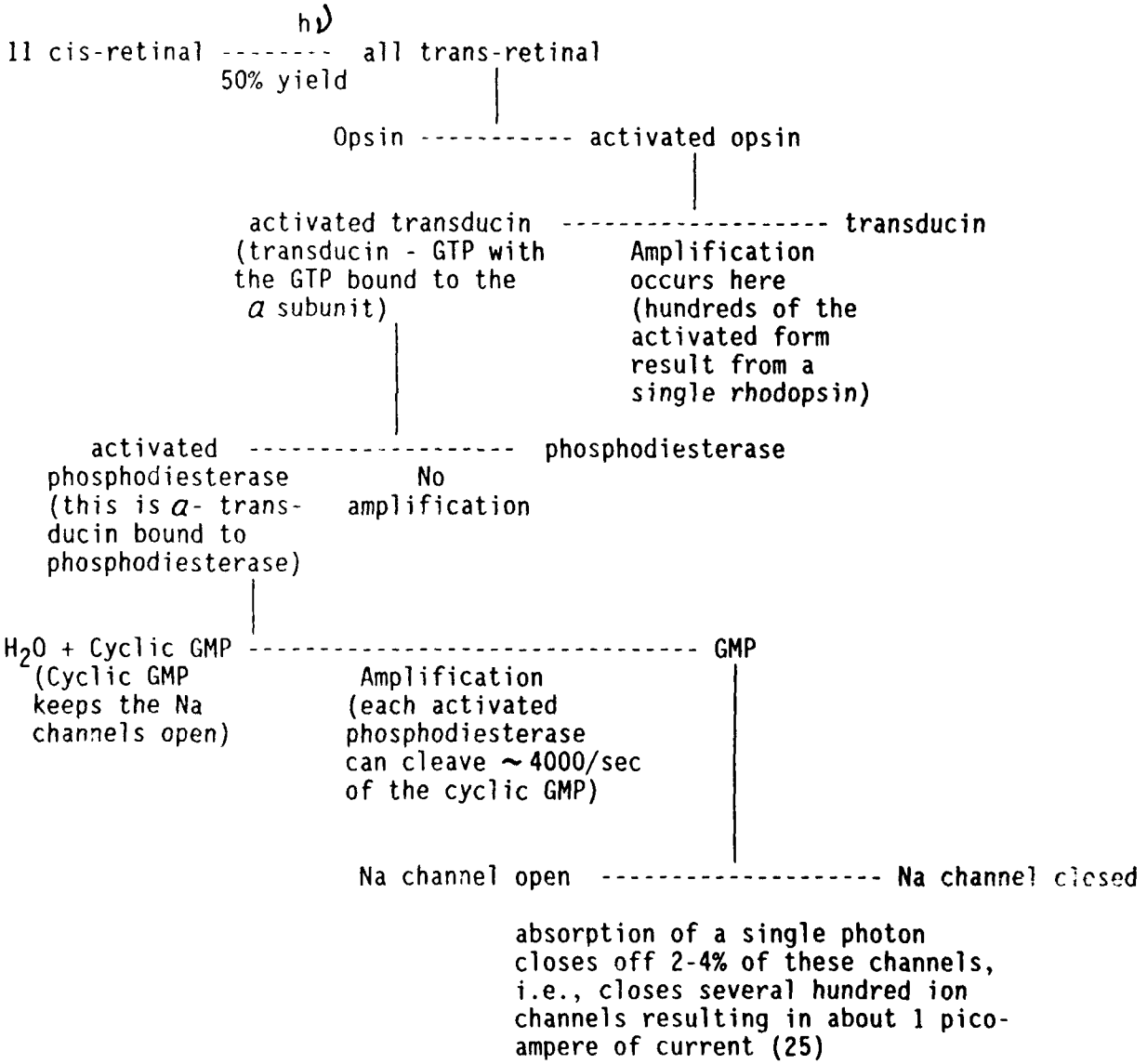
The human retina is estimated to have 10^8 rods and 3 x 10^6 cones (25). A rod may be excited by a single photon (26). Excitation is followed by a cascade of biochemical reactions. Some reactions are amplified varying the background illumination. Sensitivity of rod cells varies with the intensity of illumination, with less sensitivity in brighter light. The ROS has approximately 2000 stacked disks of membrane each with an inner cavity. Rhodopsin molecules are embedded in the membrane of each disk extending from the cytosol of the ROS to the intradiscal cavity. About 80% of ROS protein is in the form of rhodopsin (27). Each rod is estimated to contain 10^8 rhodopsin molecules (28).

Rhodopsin itself is comprised of 11-cis-retinal (a derivative of vitamin A) and opsin. Opsin is an enzyme (glycoprotein) which, as was remarked earlier, is produced in the myoid of the RIS and which moves to the ROS by way of the plasma membrane and not by way of the interior of the connecting cilium (23). Opsin has the form of seven α -helices arranged vertically in the disk membrane and connected by nonhelical segments. Coming mainly from the retinal pigment epithelium (RPE) by way of the extracellular fluid, 11-cis-retinal is attached to one of the α -helices of opsin and lies near the center of the membrane with its long axis parallel to the plane of the membrane. This enzyme is activated when its 11-cis-retinal component captures a photon and undergoes a configuration change to 11-trans-retinal. The frequency of light which 11-cis-retinal will absorb is influenced by opsin. Photoreception by rhodopsin initiates the sequence of events which leads to the propagation of a change in electrical potential from the ROS to the synaptic terminal of the rod.

The resting electrical potential on the inner surface of the ROS cell membrane is -40 mV relative to the outside of the membrane. Sodium ions flow into the ROS through sodium channels in this membrane and are pumped out of the

RIS. If this sodium ion flow into the ROS is diminished, the potential on the ROS inner surface decreases further and may reach a minimum of -80 mV. The events initiated by rhodopsin photon capture result in the closing of some of the sodium channels and hence a decrease in the inflow of sodium ions thereby changing the electrical potential of the ROS membrane (20, 25, 28).

Presently it appears that the sequence of events may be summarized as follows (25):



This process must be turned off so that it can be repeated. It seems that transducin, probably its γ - unit, is the main ingredient in the deactivation process. It is thought that calcium plays a role in modulating this process (25).

Light produces an increase in intracellular Ca^{++} and induces Ca^{++} release from the ROS in isolated retinas at the rate of about 500 Ca^{++} ions per activated rhodopsin molecule. This Ca^{++} release precedes the receptor potential (29). The intracellular source of Ca^{++} found for this process is unclear although there is Ca^{++} in the mitochondria and endoplastic reticulum.

Exposure of the dark adapted squid retina to light results in a rapid increase in its temperature (30). This heat production is dependent upon d-glucose and oxygen. The temperature rise is more than expected from the photochemical activation of rhodopsin. Suppression of the thermal response is always accompanied by suppression of the electrical response. The retinal pigment epithelium (RPE) plays a role in transferring this metabolic heat away from the photoreceptors and towards the choriocapillaris (31). A major source of this heat is most likely mitochondrial activity which produces ATP to drive the sodium pump (31).

As mentioned earlier, there are about 10^8 rhodopsin molecules in a rod and about 10^8 rods in the human retina giving a grand total of about 10^{16} rhodopsin molecules in the retina. The activation of a single rhodopsin molecule results in about 1 picoampere (i.e., 10^{-12} amperes) of current (28). There is about a 50% chance that a photon will trigger a response when absorbed. Thermal energy can activate a rhodopsin molecule. The average rate at which signals appear randomly due to false stimulus from thermal energy is one signal every 2 1/2 minutes per rod photoreceptor. For cones, it is estimated that one absorbed photon results in a photocurrent of about 10^{-14} amperes, i.e., 10 femtoamperes, with a response time four times faster than rods, i.e., 80 milliseconds for cones as compared to 300 milliseconds for rods. The electrical output of a cone that absorbs only one photon is close to the background of electrical fluctuations in its environs and therefore cannot be measured directly (28). Desensitization in rods is thought to result partly from increasing numbers of sodium channels closing in the ROS membrane as the intensity of light is increased (28). However, a decrease in open Na^+ channels is

not the only way desensitization can take place. In certain vertebrates morphological changes in the photoreceptors, called retinomotor movements, i.e., elongation and contraction (including widening of the synaptic gap), as well as migration of pigment granules in the RPE are involved in the eye's adjustment to changes in light intensity (24). However, the major source of desensitization is thought to be the neuronal processing of "impulses" produced by the photoreceptors (28).

ORDERS OF MAGNITUDE

Figure 3 is a display of (1) the lengths of some biological objects, (2) the sources and wavelengths of waves in a portion of the electromagnetic spectrum, and (3) the means to detect these various objects and wavelengths.

We have before us some provocative information. Electromagnetic radiation has been in the earth's environment since creation. Presman believes and claims to show, to some degree, that living objects exhibit a nonthermal response to electromagnetic radiation and possibly utilize it for information reception at two levels, namely, (1) from the external environment and (2) from electromagnetic radiation generated within the organism (32). If this is the case, then to avoid external noise, radiation generated, transmitted, and received entirely within the body would need to utilize the near-infrared to far ultraviolet portion of the electromagnetic spectrum since none of this portion of the spectrum penetrates into the body to any depth. Figure 3 shows the length of primary cilia and flagella within this range of the electromagnetic spectrum. These organelles have the appearance of antennae suggesting that such use of electromagnetic radiation is feasible.

QUANTUM VS. CLASSICAL

If we are to believe that magnetron-like electrical oscillatory phenomena occur in the centriole, then since size of magnetron plays a determining role in the wavelength of radiation produced, we can estimate that the centriole is producing wavelengths in the neighborhood of its diameter, 10^{-7} m. But phenomena producing wavelengths in this range are usually atomic or molecular in origin. Small magnetrons are 10^{4} times as large as centrioles. However, molecules can be as large as 10^{-1} times the size of the centriole. Since centrioles are closer in size to molecules than to magnetrons, it would seem reasonable to suspect that quantum

theory may be helpful in understanding centriole operation. But quantum electrodynamics often can be well approximated by classical electrodynamics. Which of these approaches will ultimately suffice is yet to be seen.

PROPOSAL REGARDING THE ROLE OF THE CENTRIOLE-BASAL BODY-CILIUM COMPLEX IN MAMMALIAN PHOTORECEPTORS

It is proposed that in the mammalian retinal photoreceptor, the centriole connecting the outer segment with the inner segment, serves to inhibit (filter) the spread of non-photo-induced hyperpolarized electrical potentials of the outer segment (i.e., noise) to the membrane of the inner segment and hence to the synaptic terminal.

The mechanism whereby the CBBC complex achieves this filtering effect is based upon the flow of hydrated Na^+ ions through the lumen of the basal body from the ROS to the RIS.

The flow of positively charged ions through the interior lumen of the connecting basal body (1) brings a positive charge near to the negatively charged inner surface of the plasma membrane covering the basal body and (2) allows for O-magnetron-like behavior, viz., as a backward wave tube setting up electromagnetic oscillations within this lumen.

In regard to (1) above, the screening effect of the wall of the basal body may make the Na^+ ions in the lumen of the basal body relatively ineffective in modifying the negative charge on the inner surface of the plasma membrane. Nonetheless, the tubules are composed of protein which may behave as zwitterions transferring the effect of the positive basal body to the negative inner plasma membrane surface. This should influence the electric field of the plasma membrane.

A greater influence on the plasma membrane is proposed to come from O-magnetron-like behavior. Only electromagnetic oscillations harmonic to those of the basal body lumen behaving as a BWO will pass from the ROS plasma membrane to the RIS plasma membrane. This allows only certain frequencies of plasma membrane oscillations to pass, hence filtering out much of the "electrical noise" inherent in the polarized plasma membrane.

Calcium counters the sodium ion flow through the centriole by activating the contractile elements of the inner segment. This process, too, may be graded as well as pulsa-

tile in character. Furthermore, this process, essentially induced by light but present to a much lesser extent in the dark as influenced by noise, could serve to pump nutrients from the inner segment to the outer segment.

The centriole perpendicular to the basal body of the connecting cilium serves to enhance the Na^+ flow through the basal body by using a venturi effect, its flow emanating from the mitochondrial output of ATP. Mitochondria generate heat and therefore a flow in their surrounding media. They also have their own pumping action, i.e., expansion and contraction of their volume which will contribute to movement of fluids in the environs.

A similar mechanism of operation is proposed for the primary cilia of the RPE. The increase in rootlet structure along with the increase in number of centriole-basal body-primary cilium complexes serves to increase the mobility of the RPE cell membrane according to this proposed conceptualization. The current necessary to drive this process has not been identified but could readily be Na^+ or K^+ or possibly even Ca^{++}. These primary cilia are conical, tapering distally, and may be stimulated by light passing out of the rods and cones. If the primary cilia in the RPE "light up", so to speak, then the message is received that there is not enough pigmented pseudopods to diminish the light (and heat) and hence more pigment is extended down around the photoreceptors.

REFERENCES

1. Schuschereba ST, Zwick H, Stuck BE, Beatrice ES. Basal body and striated rootlet changes in primate macular retinal pigmented epithelium after low level diffuse argon laser radiation. Presidio of San Francisco, California: Letterman Army Institute of Research, 1982; Tech. Note 82-35TN.

2. Wheatley DN. The centriole: A central enigma of cell biology. Amsterdam: Elsevier Biomedical Press, 1982:151.

3. Novikoff AB, Holtzman E. Cells and organelles. New York: Holt, Rinehart, and Winston, 1970:139.

4. Collins GB, ed. Microwave magnetrons. New York: McGraw Hill Book Company, 1948.

5. Morrier G, Okress E. Introduction. In: Okress E, ed. Crossed field microwave devices; vol 1. New York: Academic Press, 1961.

6. Lance AL. Introduction to microwave theory and measurements. New York: McGraw Hill Book Company, 1964.

7. Atwater HA. Introduction to microwave theory. New York: McGraw Hill Book Company, 1962.

8. Page L, Adams NI. Principles of electricity. New York: D. Van Nostrand Company, 1949.

9. Okress E, ed. Crossed field microwave devices. New York: Academic Press, 1961.

10. Beck AHW. Thermionic valves. Cambridge University Press, 1953.

11. Page FM, Goode GC. Negative ions and the magnetron. New York: Wiley, Interscience Division of John Wiley & Sons, 1969.

12. Stubblefield E, Brinkley BR. Architecture and function of the mammalian centriole. In: Warren KB, ed. The origin and fate of cell organelles; vol 6. New York, London: Academic Press, 1967.

13. Wolfe SL. Biology of the cell. Belmont, CA: Wadsworth Publishing Company, 1972.

14. Hartman H, Puma JP, Gurney T. Evidence for the association of RNA with the ciliary basal bodies of tetrahymena. J Cell Sci 1974;16:241-260.

15. Hartman H. The centriole and the cell. J Theoret Biol 1975;51:501-509.

16. To LP. Are centrioles semiautonoumous in endocytobiology? Ann New York Acad Sci 1987;503:88.

17. Milhaud M, Pappos GD. Cilia formation in the adult cat brain after pargyline treatment. J Cell Biol 1968;37:599-609.

18. Hubert JP, Flament-Durnad J, Dustin P. Centrioles and cilia multiplication in the pituitary of the rat after furosemide and chochicine treatment I. The posterior lobe. Cell Tiss Res 1974;149:349-361.

19. Nenci I, Marchetti E. Concerning the localization of steroids in centrioles and basal bodies by immunofluorescence. J Cell Biol 1978;76:255-260.

20. Rodieck RW. The vertebrate retina: Principles of structure and function. San Francisco: W. H. Freeman Company, 1973.

21. Schuschereba ST, Zwick H. Ciliary rootlets in primate rods and cones. Presidio of San Francisco, California: Letterman Army Institute of Research, 1982; Tech. Note No. 82-34TN.

22. Spira AW, Milman GE. Filament arrays in the photoreceptor cell of the human, monkey, and guinea pig retina. In: Hollyfield JG, Vidrio EA, eds. The structure of the eye. New York: Elsevier/North Holland, 1982:1-10.

23. Beharse JC. Photosensitive membrane turnover; Differentiated membrane domains and cell-cell interaction. In: Adler R, Farber D, eds. The retina: A model for cell biology studies. New York: Academic Press, 1986:297-352. (Part I).

24. Burnside B, Dearry A. Cell motility in the retina. In: Adler R, Farber D, (eds). The retina: A model for cell biology studies. New York: Academic Press, 1986:151-206. (Part I).

25. Stryer L. The molecules of visual excitation. Sci Am July 1987;42-50.

26. Stryer L. Transducin and the cyclic GMP phosphodiesterase; Amplifier proteins in vision. Cold Spring Harbor symposium on quantum biology. 1983:841-852.

27. Michel-Villaz M, Saibil H, Chabre M. Orientation of rhodopsin α- helices in retinal rod outer segment membranes studied by infrared linear dichroism. Proc Nat'l Acad Sci. USA (Sept) 1979:4405-4408.

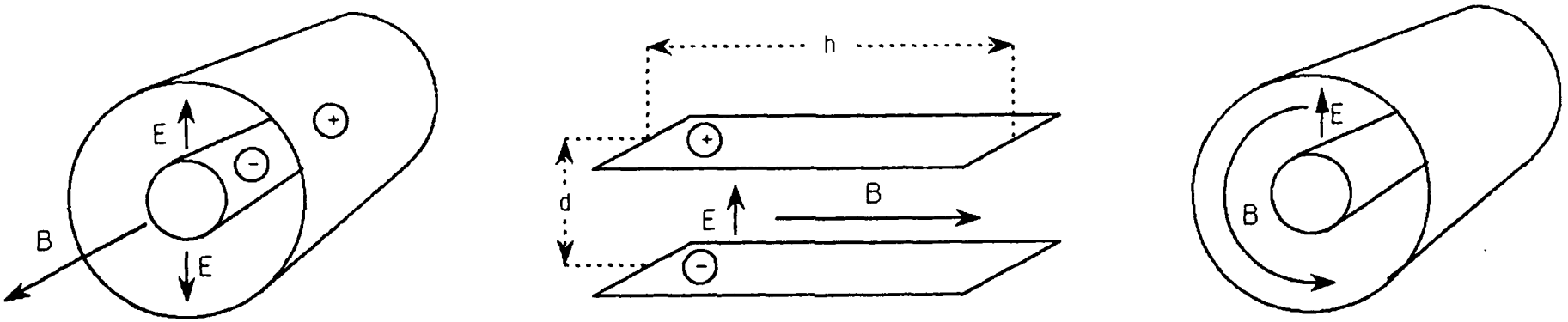
28. Schnapf J, Baylor DA. How Photoreceptor cells respond to light. Sci Am April 1987;40-47.

29. O'Brien DF. The chemistry of vision. Science 1982; 218:961-966.

30. Tasaki I, Nakaye T. Heat generated by the dark-adapted squid retina in response to light pulses. Science 1985;227:654-655.

31. Duane TD, Jaeger EA (eds). Clinical Ophthalmology; vol 3. Philadelphia: Harper and Row, 1987:4.

32. Presman AS. Electromagnetic Fields and Life. New York, London: Plenum, 1970.



(a) Cylindrical (b) Planar (c) Coaxial or Toroidal

Figure 1. Various M-magnetron Configurations

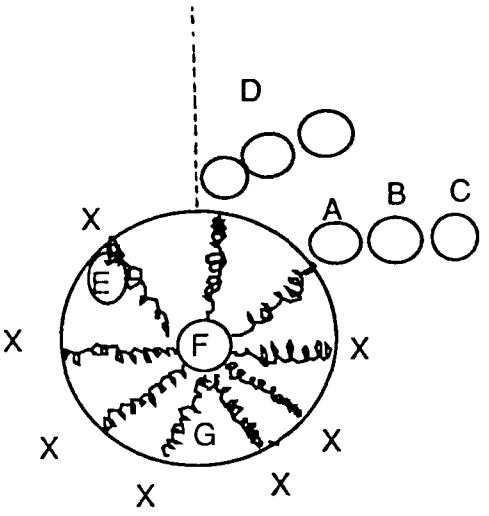


Figure 2. Cross section of a sector of the proximal portion of a centriole. (A)(B)(C): Tubules which share three molecules at each of their junctions. (D) The angle of pitch of the tubules (approximately 10^{o}). (E) Helical structure seen in the core of some centrioles. (F) Controversial central hub. (G) Electron dense cartwheel seen at the proximal end of the centriole. In some protozoan species it goes throughout the centriole. (X) Sites of tubule triplets such as A, B, C.

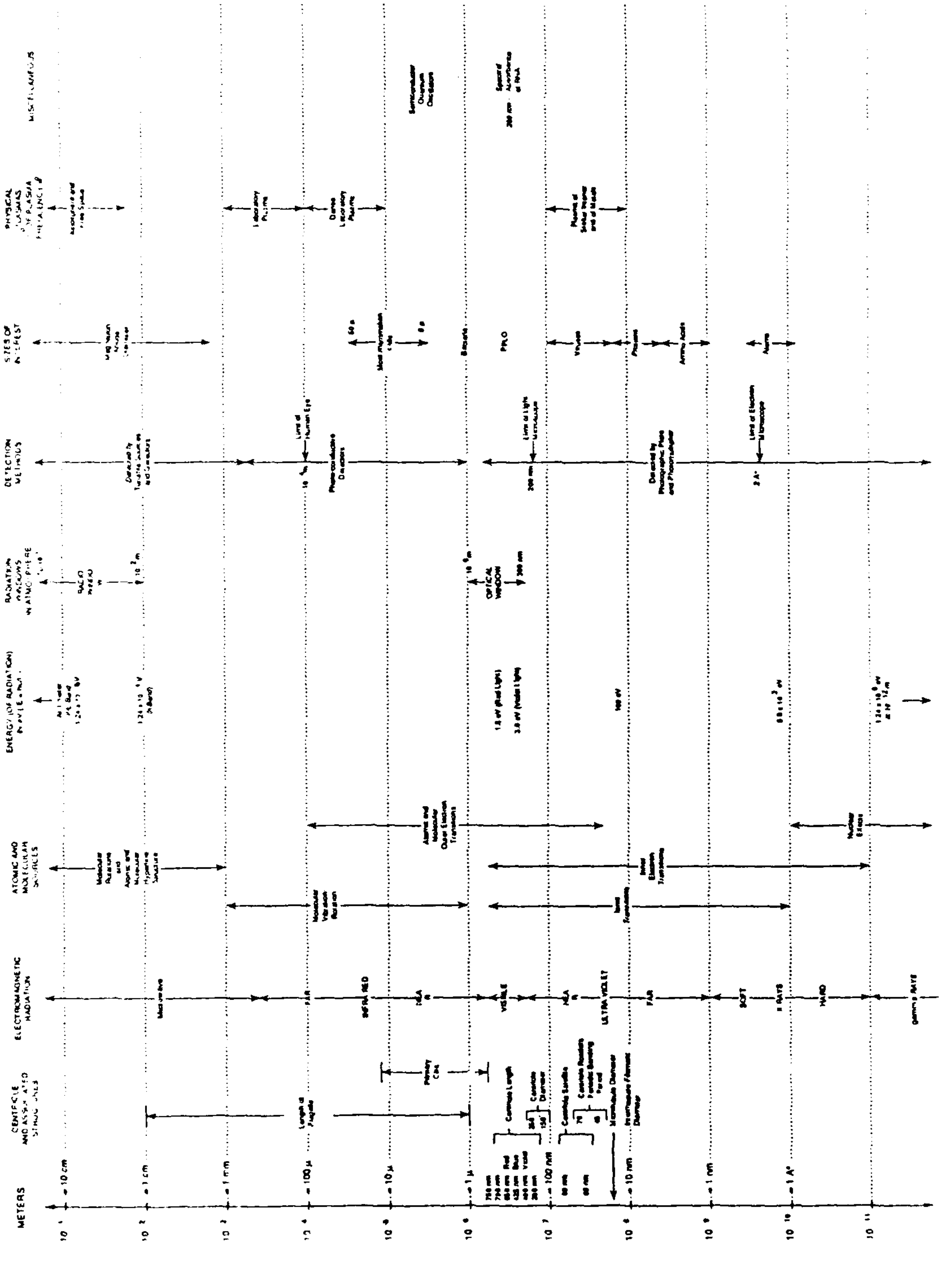


Figure 3. Orders of Magnitude

OFFICIAL DISTRIBUTION LIST

Commander
USAMRDC
ATTN:SGRD-PLC/MG Russell
ATTN:SGRD-PLC/COL Lam
SGRD-RMS/Ms. Madigan
Fort Detrick, MD 21701-5000

Director
Defense Technical Information
ATTN:DTIC-DDA (2 copies)
Cameron Station
Alexandria, VA 22314

Commander
US Army SMO
ATTN:AMXCM-EO/MAJ Dedmond
2800 Powder Mill Road
Adelphi, MD 20783

Commander
USAMSAA
ATTN: DRXSY-CSD/P. Baers
ATTN: DRXST-GWD/F. Campbell
Aberdeen Proving Ground
Maryland 21010

Commander
ATTN: AFWAL/MLPJ/G. Kepple
Wright Patterson AFB
Ohio 45433

Commander
US AEHA
ATTN: HSHB-RL/D. Sliney
Aberdeen Proving Ground
Maryland 21010

Dr. John Ewen
PO Box 1925
Washington, DC 20013

Commander
HQ, USAMMDA
ATTN: SGRD-UMA/Channing
Fort Detrick
Frederick, MD 21701-5012

Commander
ATTN:AFAMRL/HEF/R. Susnik
Wright Patterson AFB
Ohio 45433

Headquarters
Department of the Army
ATTN: DASG-TLO
Washington, DC 20310

Commander
CACDA/ATZL-OPS-SE
ATTN: MAJ J.C. Johnson
Fort Leavenworth
Kansas 66027

Director
NADC
ATTN: Code 601B/Dr. Chisum
Warminster, PA 18974-5000

Commander
NMRDC
ATTN: Code 43
National Naval Med Center
Bethesda, MD 20814

Commander
USAF SAM
ATTN: RZW/Dr. Farrer
ATTN: RZW/LTC Cartledge
Brooks AFB, Texas 78235

Official Distribution List, cont.

Director
AMSAA
ATTN: AMXSY-CR/Mr. Brand
Aberdeen Proving Ground
Maryland 21005

Commander
USA Aviation Systems Command
ATTN: AMCPM-ALSE/H. Lee
4300 Goodfellow Blvd
St. Louis, MO 63120

Director
Defense Intelligence Agency
ATTN: DT-5A/Hal Hock
Pentagon
Washington, DC 20301

Commander
USA Aeromedical Research Lab
ATTN: COL La Mothe
Ft. Rucker, AL 36330-5000

Director
EWL/RSTA Center
ATTN: AMSEL-EW-C/J. Allen
Ft Monmouth, NJ 07703-5303

Director
USA HEL
ATTN: AMXHE-IS/D. Giordano
Aberdeen Proving Ground
Maryland 21005-5001

Director
US Army AMMRC
ATTN: AMXMR-O/Fitzpatrick
Watertown, MA 02172-0001

Director
Armed Forces Medical
Intelligence Center
ATTN: AFMIC-SA/MAJ Downs
Fort Detrick
Maryland 21701-5004

Director
DTD Directorate
ATTN: EOGWCM-CCM/Kasparek
White Sands Missile Range
New Mexico 88002-5519

Commander
HQ TRADOC
ATTN: ATCD-ML/J. Gray
Ft. Monroe, VA 23651-5000

Commander
LAIR
ATTN: SGRD-ULZ (1 copy)
SGRD-IR (10 copies)
PSF, CA 94129-6800